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FILE 'HOME' ENTERED AT 13:10:57 ON 21 MAR 2003

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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FULL ESTIMATED COST                                         0.21       0.21

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS,
       ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 13:11:11 ON 21 MAR 2003
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11 FILES IN THE FILE LIST

=> s endooligopeptidase(w)'a'
FILE 'MEDLINE'
            10 ENDOOLIGOPEPTIDASE
       7035586 'A'
L1           9 ENDOOLIGOPEPTIDASE(W)'A'

FILE 'SCISEARCH'
            14 ENDOOLIGOPEPTIDASE
       8541203 'A'
L2           8 ENDOOLIGOPEPTIDASE(W)'A'

FILE 'LIFESCI'
             4 ENDOOLIGOPEPTIDASE
       1879127 'A'
L3           3 ENDOOLIGOPEPTIDASE(W)'A'

FILE 'BIOTECHDS'
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        286290 'A'
L4           0 ENDOOLIGOPEPTIDASE(W)'A'

FILE 'BIOSIS'
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L5          12 ENDOOLIGOPEPTIDASE(W)'A'

FILE 'EMBASE'
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       6183768 'A'
L6           8 ENDOOLIGOPEPTIDASE(W)'A'

FILE 'HCAPLUS'
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      16945828 'A'
L7          28 ENDOOLIGOPEPTIDASE(W)'A'

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FILE 'ESBIOBASE'
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       1757902 'A'
L9           4 ENDOOLIGOPEPTIDASE(W)'A'

FILE 'BIOTECHNO'
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L10           4 ENDOOLIGOPEPTIDASE(W)'A'

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L13           8 L1 NOT 1999-2003/PY

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L14           5 L2 NOT 1999-2003/PY

FILE 'LIFESCI'
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L15           3 L3 NOT 1999-2003/PY

FILE 'BIOTECHDS'
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L16           0 L4 NOT 1999-2003/PY

FILE 'BIOSIS'
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L17          10 L5 NOT 1999-2003/PY

FILE 'EMBASE'
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L18           6 L6 NOT 1999-2003/PY

FILE 'HCAPLUS'
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L19          22 L7 NOT 1999-2003/PY

FILE 'NTIS'
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L20           0 L8 NOT 1999-2003/PY

FILE 'ESBIOBASE'
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L21           1 L9 NOT 1999-2003/PY

FILE 'BIOTECHNO'
         484603 1999-2003/PY
L22           2 L10 NOT 1999-2003/PY

FILE 'WPIDS'
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L23           0 L11 NOT 1999-2003/PY

TOTAL FOR ALL FILES
L24          57 L12 NOT 1999-2003/PY

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PROCESSING COMPLETED FOR L24
L25          25 DUP REM L24 (32 DUPLICATES REMOVED)

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L25 ANSWER 1 OF 25 MEDLINE DUPLICATE 1
TI Species specificity of thimet oligopeptidase (EC 3.4.24.15).
SO BIOLOGICAL CHEMISTRY HOPPE-SEYLER, (1996 May) 377 (5) 283-91.
Journal code: 8503054. ISSN: 0177-3593.
AU Hayashi M A; Gomes M D; Reboucas N A; Fernandes B L; Ferro E S; de Camargo A C
AN 96426540 MEDLINE

L25 ANSWER 2 OF 25 MEDLINE DUPLICATE 2
TI Characterization of an **endooligopeptidase A**-like protein in PC12 cells: activity modulation by cAMP but not by basic fibroblast growth factor.
SO JOURNAL OF CELLULAR BIOCHEMISTRY, (1995 Feb) 57 (2) 311-20.
Journal code: 8205768. ISSN: 0730-2312.
AU Ferro E S; Tambourgy D V; Abreu P A; Camargo A C; Raw I; Ho P L
AN 95279456 MEDLINE

L25 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Rat thimet oligopeptidase: large-scale expression in Escherichia coli and characterization of the recombinant enzyme
SO Biochemical Journal (1995), 309(1), 203-7
CODEN: BIJOAK; ISSN: 0264-6021
AU McKie, Norman; Dando, Pamela M.; Brown, Molly A.; Barrett, Alan J.
AN 1995:680289 HCAPLUS
DN 123:106011

L25 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Isolation and characterization of a new bradykinin potentiating octapeptide from .gamma.-casein
SO Canadian Journal of Physiology and Pharmacology (1995), 73(1), 85-91
CODEN: CJPPA3; ISSN: 0008-4212
AU Lebrun, Ivo; Lebrun, Fabiana L. A. S.; Henriques, Olga B.; Carmona, Adriana K.; Juliano, Luiz; Camargo, Antonio C. M.
AN 1995:477555 HCAPLUS
DN 122:256993

L25 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Structural requirements of bioactive peptides for interaction with endopeptidase 22.19
SO Neuropeptides (Edinburgh, United Kingdom) (1994), 26(4), 281-7
CODEN: NRPPDD; ISSN: 0143-4179
AU Camargo, A. C. M.; Gomes, M. D.; Toffoletto, O.; Ribeiro, M. J. F.; Ferro, E. S.; Fernandes, B. L.; Suzuki, K.; Sasaki, Y.; Juliano, L.
AN 1994:316023 HCAPLUS
DN 120:316023

L25 ANSWER 6 OF 25 MEDLINE DUPLICATE 3
TI Thimet oligopeptidase--a review of a thiol dependent metallo-endopeptidase also known as Pz-peptidase endopeptidase 24.15 and endo-oligopeptidase.
SO BIOLOGICAL CHEMISTRY HOPPE-SEYLER, (1993 Feb) 374 (2) 91-100. Ref: 93
Journal code: 8503054. ISSN: 0177-3593.
AU Tisljar U
AN 93228849 MEDLINE

L25 ANSWER 7 OF 25 MEDLINE DUPLICATE 4
TI Endo-oligopeptidase A, a putative enkephalin-generating enzyme, in the vertebrate retina.
SO JOURNAL OF NEUROCHEMISTRY, (1991 Nov) 57 (5) 1643-9.
Journal code: 2985190R. ISSN: 0022-3042.
AU Ferro E S; Hamassaki D E; Camargo A C; Britto L R
AN 92014069 MEDLINE

L25 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Assay for enkephalin-generating enzyme in rat brain tissues by

high-performance liquid chromatography with postcolumn fluorescence derivatization
SO Analytical Sciences (1991), 7(4), 561-5
CODEN: ANSCEN; ISSN: 0910-6340
AU Zhang, Guo Qing; Kai, Masaaki; Ohkura, Yosuke
AN 1992:36614 HCAPLUS
DN 116:36614

L25 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Thimet oligopeptidase (EC 3.4.24.15): the same by any name? Reply to comments
SO Biochemical Journal (1991), 277(1), 295-6
CODEN: BIJOAK; ISSN: 0306-3275
AU Barrett, Alan J.
AN 1991:553586 HCAPLUS
DN 115:153586

L25 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Distinction between endo-oligopeptidase A (EC 3.4.22.19) and soluble metalloendopeptidase (EC 3.4.24.15). Comments
SO Biochemical Journal (1991), 277(1), 294-5
CODEN: BIJOAK; ISSN: 0306-3275
AU Camargo, Antonio C. M.
AN 1991:577893 HCAPLUS
DN 115:177893

L25 ANSWER 11 OF 25 MEDLINE DUPLICATE 5
TI A selective assay for **endooligopeptidase A** based on the cleavage of fluorogenic substrate structurally related to enkephalin.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1990 Dec 14) 173 (2) 647-52.
Journal code: 0372516. ISSN: 0006-291X.
AU Juliano L; Chagas J R; Hirata I Y; Carmona E; Sucupira M; Oliveira E S; Oliveira E B; Camargo A C
AN 91083650 MEDLINE

L25 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Enzymic inactivation of bradykinin by rat brain neuronal perikarya
SO Cellular and Molecular Neurobiology (1989), 9(3), 379-400
CODEN: CMNEDI; ISSN: 0272-4340
AU DelBel, Elaine A.; Padovan, Afonso P.; Padovan, Gilberto J.; Sellinger, Otto Z.; Martins, Antonio R.
AN 1990:1312 HCAPLUS
DN 112:1312

L25 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Neuropeptide-metabolizing peptidases of nervous tissue. Reply to comments
SO Journal of Neurochemistry (1989), 53(1), 315-16
CODEN: JONRA9; ISSN: 0022-3042
AU McDermott, J. R.; Mantle, D.; Lauffart, B.; Gibson, A. M.; Biggins, J. A.
AN 1989:473670 HCAPLUS
DN 111:73670

L25 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Neuropeptide-metabolizing peptidases of nervous tissue. Comments
SO Journal of Neurochemistry (1989), 53(1), 315
CODEN: JONRA9; ISSN: 0022-3042
AU Camargo, A. C. M.
AN 1989:473535 HCAPLUS
DN 111:73535

L25 ANSWER 15 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI INTERACTION OF DYNORPHIN A DERIVED PEPTIDES WITH **ENDOOLIGOPEPTIDASE A**.

SO TWELFTH MEETING OF THE INTERNATIONAL SOCIETY FOR NEUROCHEMISTRY, ALGARVE, PORTUGAL, APRIL 23-28, 1989. J NEUROCHEM. (1989) 52 (SUPPL), S75.
CODEN: JONRA9. ISSN: 0022-3042.
AU TOFFOLETTO O; ROSSIER J; CAMARGO A C M
AN 1989:440035 BIOSIS

L25 ANSWER 16 OF 25 MEDLINE DUPLICATE 6
TI **Endooligopeptidase A** activity in rabbit heart: generation of enkephalin from enkephalin containing peptides.
SO PEPTIDES, (1988 Sep-Oct) 9 (5) 945-55.
Journal code: 8008690. ISSN: 0196-9781.
AU Cicilini M A; Ribeiro M J; de Oliveira E B; Mortara R A; de Camargo A C
AN 89220542 MEDLINE

L25 ANSWER 17 OF 25 MEDLINE DUPLICATE 7
TI Purification and characterization of bradykinin-hydrolyzing enzyme from 2-day-old rat epidermis.
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1988 May 12) 965 (2-3) 176-84.
Journal code: 0217513. ISSN: 0006-3002.
AU Kikuchi M; Fukuyama K; Epstein W L
AN 88209612 MEDLINE

L25 ANSWER 18 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI ENKEPHALIN IS LIBERATED FROM METORPHAMIDE AND DYNORPHIN A-1-8 BY **ENDOOLIGOPEPTIDASE A** BUT NOT BY METALLOENDOPEPTIDASE EC 3.4.24.15.
SO BIOCHEM J, (1988) 252 (1), 35-38.
CODEN: BIJOAK. ISSN: 0306-3275.
AU TOFFOLETTO O; METTERS K M; OLIVEIRA E B; CAMARGO A C M; ROSSIER J
AN 1988:333888 BIOSIS

L25 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Brain endo-oligopeptidase A, a putative enkephalin-converting enzyme
SO Journal of Neurochemistry (1987), 48(4), 1258-63
CODEN: JONRA9; ISSN: 0022-3042
AU Camargo, Antonio C. M.; Oliveira, Eduardo B.; Toffoletto, Odaly; Meeters, Kathleen M.; Rossier, Jean
AN 1987:454553 HCAPLUS
DN 107:54553

L25 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI A processing enzyme for prodynorphin derived peptides
SO NIDA Research Monograph (1986), 75(Prog. Opioid Res.), 247-50
CODEN: MIDAD4; ISSN: 0361-8595
AU Metters, Kathleen M.; Rossier, Jean; Oliveira, Eduardo E.; Toffoletto, Odaly; Camargo, Antonio C. M.
AN 1987:547672 HCAPLUS
DN 107:147672

L25 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Conversion and inactivation of opioid peptides by rabbit brain endo-oligopeptidase A
SO Biochemical and Biophysical Research Communications (1985), 130(2), 932-8
CODEN: BBRCA9; ISSN: 0006-291X
AU Camargo, Antonio C. M.; Ribeiro, Maria J. V. F.; Schwartz, William N.
AN 1985:535494 HCAPLUS
DN 103:135494

L25 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Degradation of neurotensin by rabbit brain endo-oligopeptidase A and endo-oligopeptidase B (proline-endopeptidase)
SO Biochemical and Biophysical Research Communications (1983), 116(3), 1151-9
CODEN: BBRCA9; ISSN: 0006-291X
AU Camargo, Antonio C. M.; Caldo, Hildeberto; Emson, Piers C.

AN 1984:19745 HCAPLUS
DN 100:19745

L25 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2003 ACS
TI Developmental changes of endooligopeptidases (kininases) in rabbit brain
SO Advances in Experimental Medicine and Biology (1983), 156B(Kinins-3, Pt. B), 863-6
CODEN: AEMBAP; ISSN: 0065-2598
AU Rino, S. M.; Camargo, A. C. M.
AN 1983:403453 HCAPLUS
DN 99:3453

L25 ANSWER 24 OF 25 MEDLINE DUPLICATE 8
TI Purification of rabbit brain endooligopeptidases and preparation of anti-enzyme antibodies.
SO BIOCHEMISTRY, (1981 Dec 8) 20 (25) 7082-8.
Journal code: 0370623. ISSN: 0006-2960.
AU Carvalho K M; Camargo A C
AN 82091832 MEDLINE

L25 ANSWER 25 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI INHIBITION OF RABBIT TISSUE KININASE BY ANTI ENDO OLIGO PEPTIDASE A ANTIBODIES.
SO BIOCHEM J, (1981) 197 (1), 85-94.
CODEN: BIJOAK. ISSN: 0306-3275.
AU COELHO H L L; CICILINI M A; CARVALHO K M; CARVALHO I F; CAMARGO A C M
AN 1982:214813 BIOSIS

=> d ab tot

L25 ANSWER 1 OF 25 MEDLINE DUPLICATE 1
AB The recombinant rat testes metallo-endooligopeptidase (EC 3.4.24.15) and the rabbit brain **endooligopeptidase A** (formerly EC 3.4.22.19) were compared, side-by-side, in view of their striking similarities in both the physicochemical features and the specificities for oligopeptides. Concerning the tissue distribution in rat and rabbit, no relation between the levels of enzyme activity in cytosol and the levels of metallo-endooligopeptidase 24.15 mRNA could be established. The results suggest that the predominant neuropeptide-metabolizing activity attributed to the metallo-endooligopeptidase 24.15 is performed by, at least, two distinct cytosolic enzymes, one predominant in rat testes and the other in rabbit brain and testes, and possibly also in rat brain. Both enzymes are activated by dithiothreitol and irreversibly inhibited by a SH-affinity labeling dynorphin-related compound, but they are not inhibited by EDTA in a concentration dependent manner. Both enzymes exhibit the same specificity toward several bioactive peptides, except for LH-RH and substance P, which are only hydrolysed by the rat testes enzyme. Taken together, these results lead us to conclude that it is unlikely that the recombinant rat testes metallo-endooligopeptidase 24.15 and the rabbit brain **endooligopeptidase A** are the same molecule although they might belong to the same family of oligopeptidases.

L25 ANSWER 2 OF 25 MEDLINE DUPLICATE 2
AB **Endooligopeptidase A** is a putative neuropeptide-metabolizing enzyme. It converts small enkephalin-containing peptides into the corresponding enkephalins and inactivates biopeptides such as bradykinin and neurotensin in vitro. We investigated the presence of **endooligopeptidase A** in PC12 cells. This cell line was derived from a rat pheochromocytoma tumor and resembles fetal chromaffin cell. Depending on the supplements added to the cell culture, this cell line can be differentiated into mature chromaffin cell or sympathetic neuron-like cell. **Endooligopeptidase A** activity was measured in soluble cellular extracts using a specific

fluorogenic substrate QF-ERP7. The PC12 **endooligopeptidase A**-like activity shared similar but not identical biochemical properties with rabbit brain **endooligopeptidase A**. Similarly to rabbit brain **endooligopeptidase A**, the PC12 **endooligopeptidase A**-like activity was enhanced by DTT, totally inhibited by DTNB and 1-10 Phenanthroline, partially inhibited by cFP-AAF-pAb, and not affected by PMSF. Furthermore, the PC12 **endooligopeptidase A**-like activity displayed identical elution profile as rabbit brain **endooligopeptidase A** in gel filtration and anion-exchange chromatography. In addition, an antiserum raised against rabbit brain **endooligopeptidase A** cross-reacted with a 71 kDa component from PC12 cell extracts in Western blotting and was also able to partially neutralize the PC12 **endooligopeptidase A**-like activity. Treatment of PC12 cells with basic fibroblast growth factor (bFGF), a neurotrophic factor for this cell line, did not modify the specific activity of this enzyme. However, cAMP analogs decreased the specific activity of the enzyme. These results indicate the presence of an **endooligopeptidase A** -like activity in PC12 cells which is modulated by cAMP but not by bFGF.

L25 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB The coding sequence for rat testis thimet oligopeptidase (EC 3.4.24.15) (I) was placed under the control of the phage T7 DNA polymerase/promoter system. Cultures of E. coli transfected with the resulting plasmid expressed I as a sol. cytoplasmic protein. Medium-scale cultures allowed isolation of I in quantities of tens of milligrams. The availability of recombinant I permitted the detn. of such chem. properties, as .epsilon.280 (48,960), Zn content (2 atom/mol.), and available SH group content (8-10/mol.) for I. Recombinant I showed the catalytic activities previously reported for the naturally occurring enzyme, so that it could be concluded with confidence that these are all due to I and there is no need to postulate the existence of sep. Pz-peptidase or **endooligopeptidase A** activities.

L25 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB This paper describes the isolation and sequencing of a novel bradykinin-potentiating peptide, generated by tryptic hydrolysis of the .gamma.-casein chain. No homol. was found to other known vasoactive or vasopotentiating peptides. The octapeptide Tyr-Pro-Val-Gln-Pro-Phe-Thr-Glu, corresponding to the .gamma.-casein(114-121) sequence, was isolated from the tryptic hydrolysis of .gamma.-casein and also synthesized by solid-phase peptide synthesis. Both natural and synthetic peptides had the same retention time in HPLC and displayed a selective potentiating activity on isolated guinea-pig ileum for bradykinin and Lys-bradykinin but were not able to potentiate the effects of Met-Lys-bradykinin, Ile-Ser-bradykinin, angiotensin II, acetylcholine, or histamine. I.v. injections of bradykinin and of bradykinin-potentiating octapeptide produced a persistent hypotension in conscious rats, a pattern that was not obtained when the octapeptide was replaced by captopril. This bradykinin-potentiating octapeptide is a strong competitive inhibitor of **endooligopeptidase A** (EC 3.4.24.15, formerly EC 3.4.22.19), but it has low inhibitory potency towards angiotensin-converting enzyme (EC 3.4.15.1). Thus, the results suggest that other peptidases in addn. to angiotensin-converting enzyme, such as endo-oligopeptidase A, may contribute to the redn. of the effective concn. of bradykinin in the circulation.

L25 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB A series of biol. active peptides and related compds. (opioid peptides, neurotensin, and bradykinin) were used as substrates or competitive inhibitors to study the structural requirements for peptide interaction with endopeptidase 22.19. The kinetics of hydrolysis of these peptides indicated that, in contrast to other proteinases, the substrate specificity of endopeptidase 22.19 is not detd. by the amino acids

flanking the sensitive bonds of the substrates. The competition between bioactive peptide analogs and the quenched fluorescence substrate of endopeptidase 22.19 indicated that their length and their flexibility may be the dominant factors to explain their binding specificities. These peculiar features of endopeptidase 22.19 may be of importance to understand the physiol. process of conversion and inactivation of biol. active peptides.

L25 ANSWER 6 OF 25 MEDLINE DUPLICATE 3
AB Thimet oligopeptidase (EC 3.4.24.15) is a thiol-dependent metallo-endopeptidase also known as Pz-peptidase, collagenase-like peptidase, **endooligopeptidase A**, soluble metallo-endopeptidase and endopeptidase 24.15. The enzyme is closely related to the yeast proteinase yscD. Thimet oligopeptidase (M(r) 74000) is widely distributed in animals and plants. In rat liver it exists in a cytoplasmic and mitochondrial form; a membrane-bound form of the enzyme was discovered in rat brain. Thimet oligopeptidase hydrolyses small peptides but does not act on proteins. In rat brain thimet oligopeptidase is involved in the generation of enkephalins and inactivation of bioactive peptides and experiments with yeast provided good evidence that the enzyme is involved in the late stages of cytoplasmatic protein degradation.

L25 ANSWER 7 OF 25 MEDLINE DUPLICATE 4
AB Endo-oligopeptidase A, EC 3.4.22.19, converts small enkephalin-containing peptides into the corresponding enkephalins in vitro. We investigated the presence of **endooligopeptidase A** in the retina and its possible colocalization with enkephalins in retinal neurons. The specific activity of endo-oligopeptidase. A found in pigeon retinae (30.3 +/- 7.3 mU/mg, mean +/- standard deviation) was four times higher than in rabbit retinae (7.0 +/- 1.1 mU/mg). The enzyme activity was not modified by EDTA, but it was enhanced by dithiothreitol and inhibited by zinc and 5,5'-dithiobis(2-nitrobenzoic acid). Immunohistochemical experiments with a purified antiserum against rabbit endo-oligopeptidase A revealed labeled neurons in both the inner nuclear layer and the ganglion cell layer of pigeon and rabbit retinae. Double-labeling immunofluorescence experiments demonstrated that about 90% of neurons containing endo-oligopeptidase A-like immunoreactivity also contained [Leu5]-enkephalin-like immunoreactivity. These colocalization results may represent an important step toward the demonstration of the possible involvement of endo-oligopeptidase A in enkephalin generation in vivo.

L25 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB A simple and sensitive method for assaying enkephalin-generating enzyme activity in rat brain tissues is described. Methionine-enkephalin, produced enzymically from .alpha.-endorphin and BAM-12P as substrates, and leucine-enkephalin, produced from .alpha.-neoendorphin, were quantified by HPLC with postcolumn fluorescence derivatization using hydroxylamine, cobalt(II), and borate. The detection limits for methionine- and leucine-enkephalin-generating activities of the enzyme are 2.5 and 3.0 pmol min-1 mg protein-1, resp. The enzyme can be characterized as an endo-oligopeptidase A-like enzyme on the basis of inhibition studies.

L25 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB A polemic in response to A. C .M. Camargo (ibid. 294), with respect to whether **endooligopeptidase A**, Pz peptidase, and sol. metalloendopeptidase embrace 1 or several enzymes, is given. Thimet oligopeptidase is favored as an alternative name for sol. metalloendopeptidase (EC 3.4.24.15); thimet is an acronym for thiol-dependent metallo-, and oligopeptidase reflects the selectivity of the enzyme for substrates of .apprx.5-15 amino acid residues.

L25 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB A polemic in response to A.J. Barrett and M.A. Brown (ibid., 1990, 271, 701-706). Their conclusion that brain endo-oligopeptidase A,

metalloendopeptidase, and Pz-peptidase are due to 1 enzyme is not supported by other exptl. data, including chromatog. sepn. of the activities.

L25 ANSWER 11 OF 25 MEDLINE DUPLICATE 5
AB A novel quenched fluorescence substrate, QF-ERP7 (Abz-G-G-F-L-R-R-V-EDDn), structurally related to enkephalins, proved to be suitable for assaying the **endooligopeptidase A** (E.C.3.4.22.19) activity. The enzyme only splits the L-R bond (Km 1.75 microM, Kcat 8.25 s-1), a reaction efficiently blocked by anti-**endooligopeptidase A** antibodies and by inhibitor and alternative substrates of the enzyme. Evidences based on the action of inhibitors and on the analysis of QF-ERP7 fragments demonstrated that **endooligopeptidase A** contributes with 100% of the QF-ERP7 cleaving activity found in the cytosol of rabbit brain homogenates and with 85% of that recovered in the membrane fraction. Homologous substrates, Abz-G-G-F-L-R-R-EDDn and Abz-G-G-F-L-R-EDDn, were resistant to hydrolysis. The convenience and sensitivity of the fluorimetric assay based on the QF-ERP7 moiety offers several advantages compared with previously described painstaking procedures for **endooligopeptidase A** activity measurements, what will certainly contribute to further our understanding of the role of this enzyme on the peptide hormone metabolism.

L25 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB Bradykinin (Bk; Arg1-Pro2-Pro3-Lgy4-Phe5-Ser6-Pro7-Phe8-Arg8) inactivation by bulk isolated neurons from rat brain is described. Bk is rapidly inactivated by neuronal perikarya (4.2 fmol/min/cell body). Sites of inactivating cleavages, detd. by a kininase bioassay combined with a time-course Bk-product anal., were the Phe5-Ser6, Pro7-Phe8, Gly4-Phe5, and Pro3-Gly4 peptide bonds. The cleavage of the Phe5-Ser6 bond inactivated Bk at least 5-fold faster than the other obsd. cleavages. Inactivating peptidases were identified by the effect of inhibitors on Bk-product formation. The Phe5-Ser6 bond cleavage is attributed mainly to a Ca-activated thiol-endopeptidase, a predominantly sol. enzyme which did not behave as a metalloenzyme upon dialysis and was strongly inhibited by N-[1(R,S)-carboxy-2-phenylethyl]-Ala-Ala-Phe-p-aminobenzoate and **endooligopeptidase A** antiserum. Thus, neuronal perikarya thiol-endopeptidase seems to differ from endo-oligopeptidase A and endopeptidase 24.15. Endopeptidase 24.11 cleaves Bk at the Gly4-Phe5 and, to a larger extent, at the Pro7-Phe8 bond. The latter bond is also cleaved by angiotensin-converting enzyme (ACE) and prolyl endopeptidase (PE). PE also hydrolyzes Bk at the Pro3-Gly4 bond. Secondary processing of Bk inactivation products occurs by a rapid cleavage of Ser6-Pro7-Phe8-Arg8 at the Pro7-Phe8 bond by endopeptidase 24.11, 3820ACE, and PE; a bestatin-sensitive breakdown of Phe8-Arg9; and conversion of Arg1-Pro7 to Arg1-Phe5, of Gly4-Arg9 to both Gly4-Pro7 and Ser6-Arg9, and of Phe5-Arg9 to Ser6-Arg9, Phe8-Arg9, and Ser6-Pro7, by unidentified peptidases. A model for the enzymic inactivation of bradykinin by rat brain neuronal perikarya is proposed.

L25 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB A polemic in response to A. C. M. Camargo (ibid., 1989, 315, 53) is given. The contention that the endopeptidase activity attributed to arginylaminopeptidases of human brain is due to contamination with endoligopeptidase A is not supported by the results, particularly sensitivity of the endopeptidase to EDTA and the inability to sep. endopeptidase activity from arginylaminopeptidase by a variety of electrophoretic and chromatog. techniques. It is contended that the evidence is against the endopeptidase activity assocd. with arginylpeptidase being a contaminant and that the endopeptidase resembles the metallopeptidase EP 24.15 more closely than the cysteine-dependent **endooligopeptidase A**.

L25 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AB A polemic. The report of J. R. McDermott et al. (ibid, 1988, 50, 176-82) of endopeptidase activity assocd. with arginylaminopeptidases of human brain may be explained by contamination with the previously described endoolidopeptidase A. The properties of the endopeptidase described correspond quite closely to those of this enzyme.

L25 ANSWER 15 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

L25 ANSWER 16 OF 25 MEDLINE DUPLICATE 6
AB Two endopeptidases displaying similar specificities towards peptide hormone substrates but differing in molecular size have been identified in rabbit heart and isolated by a combination of ion-exchange chromatography, gel filtration and preparative gel electrophoresis. These two enzymes share several properties with the previously described rabbit brain **endooligopeptidase A**. They were shown to produce, by a single peptide bond cleavage, [Met5] enkephalin and [Leu5]enkephalin from small enkephalin containing peptides. They also hydrolyze the Phe5-Ser5 bond of bradykinin and the Arg8-Arg9 bond of neurotensin. Characteristically, the activity of both low and high Mr enzymes is restricted to oligopeptides. Both forms of heart **endooligopeptidase A** are inhibited by antibodies raised against the brain enzyme. When electrophoresed in SDS-polyacrylamide gel under denaturing conditions, the low Mr heart enzyme shows a major band of Mr = 73,000, comparable in size to the brain enzyme. The SDS-PAGE of the high and low Mr enzymes analyzed by immunoblotting with an antibody raised against low Mr brain **endooligopeptidase A**, showed a major antigen band corresponding to Mr = 72,000. In addition, immunoblotting has also demonstrated that a monoclonal antibody antitubulin reacts with a polypeptide corresponding to Mr = 50,000 present in the purified high Mr **endooligopeptidase A**. Both enzymes are activated by dithiothreitol and inhibited by thiol reagents, but are not affected by leupeptin, DFP or EDTA, thus indicating that they should be classified as nonlysosomal cysteinyl-**endooligopeptidase A**.

L25 ANSWER 17 OF 25 MEDLINE DUPLICATE 7
AB Bradykinin-hydrolyzing enzyme was purified 200-fold from a soluble fraction of cornified cells from 2-day-old rat epidermis. The enzyme has an Mr of 80,000 as identified by SDS polyacrylamide gel electrophoresis and HPLC gel filtration. The isoelectric point of the enzyme is 5.05. The enzyme hydrolyzed Phe5-Ser6 of bradykinin and seven bradykinin-related peptides, and Tyr5-Ser6 of Tyr5-bradykinin. Production of bradykinin fragments, Arg-Pro-Pro-Gly-Phe and Ser-Pro-Phe-Arg, proceeded in a stoichiometric fashion. Km and Vmax values for bradykinin were 33 microM and 22.2 mumol/min per mg, respectively. The enzyme did not hydrolyze azocasein, denatured hemoglobin or synthetic substrates for other epidermal proteinases. The enzyme activity was enhanced by reducing agents and inhibited by sulfhydryl-blocking agents and divalent cations. Diisopropyl fluorophosphate and phenylmethylsulfonyl fluoride had no effects. The enzyme has a pH optimum of 7.0-7.5 and is stable at 4 degrees C for 1 month, but loses activity completely at 60 degrees C for 10 min. The epidermal endopeptidase differs in several properties from **endooligopeptidase A** purified from brain which hydrolyzes Phe5-Ser6 of bradykinin.

L25 ANSWER 18 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AB It has been previously reported that both the cysteinyl-endo-oligopeptidase A and the metalloendopeptidase EC 3.4.24.15 are able to generate enkephalin from a number of enkephalin-containing peptides, including dynorphin A1-8. The present study shows that only endo-oligopeptidase A is able to generate [Leu5]enkaphalin and [Met5]enkephalin from dynorphin A1-8 and from metorphamide respectively. It is also shown that endo-oligopeptidase A neither hydrolyses the specific EC 3.4.24.15 substrate .alpha.-N-benzoyl-Gly-Ala-Ala-Phe

p-aminobenzoate, nor is inhibited by the specific EC 3.4.24.15 inhibitor N-[1(RS)-carboxy-2-phenylethyl]-.alpha.-Ala-Ala-Phe p-aminobenzoate.

L25 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB Endo-oligopeptidase A, highly purified from the cytosol fraction of bovine brain by immunoaffinity chromatog., has been characterized as a thiol endopeptidase. This enzyme, known to hydrolyze the Phe5-Ser6 bond of bradykinin and the Arg8-Arg9 bond of neurotensin, has been shown to produce, by a single cleavage, Leu5-enkephalin or Met5-enkephalin from small enkephalin-contg. peptides. Enkephalin formation could be inhibited in a concn.-dependent manner by the alternative substrate bradykinin. The optimal substrate size was found to be 8-13 amino acids, with enkephalin the only product released from precursors in which this sequence is immediately followed by a pair of basic residues. However, the specificity consts. (kcat/Km) obtained for endo-oligopeptidase A hydrolysis of bradykinin, neurotensin, and dynorphin B are of the same order, a result indicating that the substrate amino acid sequence is not the only factor detg. the cleavage site of this enzyme.

L25 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB Endo-oligopeptidase A, known to hydrolyze the Phe5-Ser6 bond of bradykinin and the Arg8-Arg9 bond of neurotensin, has been shown to produce, by a single cleavage, leucine5-enkephalin from small prodynorphin-derived enkephalin-contg. peptides. The specificity consts. (kcat/km) obtained for the hydrolysis of bradykinin, neurotensin, and dynorphin B are of the same order, suggesting that the substrate amino acid sequence is not the only factor detg. the cleavage site of this enzyme.

L25 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB The conversion of BAM-12P [75513-71-2] to methionine-enkephalin [58569-55-4] and the hydrolysis of the Phe-Met and Phe-Leu bonds of Met-enkephalin-Arg-Phe [73024-95-0] and Leu-enkephalin-Arg-Arg [77101-32-7], resp., by rabbit brain endo-oligopeptidase A [79955-97-8] were demonstrated. Peptide fragments were isolated by HPLC and identified by amino acid anal. BAM 22P [76622-26-9] was not hydrolyzed by the enzyme. The concn. dependent inhibition of BAM-12P conversion into methionine-enkephalin by bradykinin [58-82-2] and vice-versa provided addnl. evidence that endo-oligopeptidase A cleaves both the Phe5-Ser6 bond in bradykinin and the Met5-Arg6 bond of BAM-12P.

L25 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB The degrdn. of neurotensin and D-Tyr11-neurotensin by apparently homogeneous prepns. of rabbit brain **endooligopeptidase A** (I) and endooligopeptidase B (proline endopeptidase) (II) was studied. Peptide fragments were isolated by high-performance liq. chromatog. and identified by amino acid anal. I cleaved neurotensin at the Arg8-Arg9 bond, whereas D-Tyr11-neurotensin was not significantly hydrolyzed. II cleaved at the carboxyl side of Pro7, Pro10 in neurotensin and at Pro7 in D-Tyr11-neurotensin. The concn.-dependent inhibition of neurotensin degrdn. by bradykinin and vice-versa represented addnl. evidence that I cleaves both the Phe5-Ser6 bond of bradykinin and the Arg8-Arg9 bond of neurotensin.

L25 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AB Kininase activity from rabbit brains removed from animals at several time intervals, from 10 days of prenatal age to 1095 days of postnatal age, exhibited a mean of 3.5 milliunits/mg tissue in the supernatant with a max. of 5.1 milliunits/mg and a min. of 2.1 milliunits/mg. Activity in the supernatant exhibited peaks at 5, 20, 60, and 190 days of postnatal age and was lowest at 120 and 1095 days. Mean kininase activity in the particulate fraction was 0.8 milliunits/mg with the highest value (1.0 milliunits/mg) at 60 days and the lowest (0.2 milliunits/mg) at 1095 days. Antibody inhibition of kininase activity in the supernatant indicated that **endooligopeptidase A** accounts for the entire kininase

activity in prenatal, 1-yr-old, and 3-yr-old brains. Endooligopeptidase B appears at birth and remains present until 180 days.

L25 ANSWER 24 OF 25 MEDLINE DUPLICATE 8

AB **Endooligopeptidase A** was purified approximately 3 000-fold and endooligopeptidase B approximately 1200-fold from the 25 000g supernatant fraction of rabbit brain homogenate. The purified enzymes were homogeneous on the basis of acrylamide gel electrophoresis under denaturing and nondenaturing conditions, isoelectric focusing, immunochemical criteria, and specific activities of the elution profile of gel filtration on Sephadex G-100. The only peptide bond cleaved by **endooligopeptidase A** in bradykinin, Arg1-Pro2-Pro3-Gly4-Phe5-Ser6-Pro7-Phe8-Arg9, is Phe5-Ser6, whereas endooligopeptidase B hydrolyzes the Pro7-Phe8 peptide bond of bradykinin and the Pro3-Gly4 bond of des-Phe8-Arg9-bradykinin. The specific activity of the homogeneous enzymes using bradykinin as substrate was 1087 nmol min-1 mg-1 for **endooligopeptidase A** and 292 nmol min-1 mg-1 for endooligopeptidase B. Gel filtration suggested molecular weights of 75 000 and 68 000 for endooligopeptidases A and B, respectively. Sodium dodecyl sulfate gel electrophoresis suggested that each endooligopeptidase consisted of a single polypeptide chain with molecular weights of 74 000 and 69 000 for the A and B enzymes, respectively. Purified **endooligopeptidase A** or B injected into goats produces monospecific antisera directed against each enzyme. The antibody prepared against each endooligopeptidase did not react with or inhibit the activity of the other enzyme.

L25 ANSWER 25 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AB Highly purified rabbit brain endo-oligopeptidase A injected into goats produced, after 60 days of immunization, antisera that specifically inhibit purified rabbit brain **endooligopeptidase A**. An immunoreactive kiniase having the same specificity as rabbit brain endo-oligopeptidase A for bradykinin was detected in several rabbit tissues. The highest amount of this immunoreactive kininase was found in the 25,000 g supernatant fraction (S fraction) of heart, liver, skeletal muscle, ovary, brain and testis homogenates, corresponding to 89, 86, 78, 59, 56 and 53%, respectively, of the whole kininase activity found in the S fraction.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	58.71	58.92

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.11	-9.11

STN INTERNATIONAL LOGOFF AT 13:15:00 ON 21 MAR 2003

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	0	endooliogopeptidase sp	USPAT; US-PGPUB	2003/03/21 12:58
2	L2	5	endooligopeptidase	USPAT; US-PGPUB	2003/03/21 12:58

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ABSTRACT:

This invention relates to newly identified prostate or prostate cancer related polynucleotides, the polypeptides encoded by these polynucleotides herein collectively referred to as "prostate cancer antigens," and to the complete gene sequences associated therewith and to the expression products thereof, and to antibodies that immunospecifically bind these polypeptides, as well as the use of such prostate cancer polynucleotides, antigens, and antibodies for detection, prevention, prognosis, and treatment of disorders of the reproductive system, particularly disorders of the prostate, including, but not limited to, the presence of prostate cancer and prostate cancer metastases. More specifically, isolated prostate cancer nucleic acid molecules are provided encoding novel prostate cancer polypeptides. Novel prostate cancer polypeptides and antibodies that bind to these polypeptides are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human prostate cancer polynucleotides, polypeptides, and/or antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to the prostate, including prostate cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The invention further relates to methods and/or compositions for inhibiting or promoting the production and/or function of the polypeptides of the invention.

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Summary of Invention - Table CWU - BSTL:

662 841173 spermidine synthase [Homo sapiens] gi.vertline.338394 2 931 97 97 HCHBQ07 >pir.vertline.A32610.vertline.A32610 spermidine synthase (EC 2.5.1.16)-human Length = 302 663 841176 561 683 HCF0136 664 841178 thyroid receptor interactor [Homo sapiens] gi.vertline.703110 65 460 99 100 HCGBQ34 Length = 152 665 841180 (AF029777) hGCN5 [Homo sapiens] gi.vertline.3220164 553 1530 97 97 HCGLC82 >sp.vertline.G3220164.vertline.G3220164 HGCN5. >gi.vertline.1491935 histone acetyltransferase [Homo sapiens][SUB 362-837] >sp.vertline.G1911495.vertline.G1911495 HGCN5=TRANSCRIPTIONAL ADAPTOR. [SUB 411-837] Length = 837 666 841181 2 283 HCFMN22 667 841182 70K protein (AA 1-614) [Homo sapiens] gi.vertline.36100 251 988 100 100 HCFNJ56 >pir.vertline.A25707.vertline.A25707 U1 snRNP 70K protein- human >gi.vertline.337447 small ribonucleoprotein 70 kd protein [Homo sapiens] [SUB 178-614] >gi.vertline.602021 hU1-70K protein (302 AA) [Homo sapiens] [SUB 227-527] Length = 614 668 841185 342 536 HCFNF67 669 841187 458 1096 HCGAA74 670 841188 DNA repair endonuclease subunit [Homo gi.vertline.1524411 2 2749 92 92 HCFMK76 sapiens] Length = 905 671 841189 336 926 HCFMC34 672 841192 methylmalonyl-CoA mutase [Homo sapiens] gi.vertline.187452 1 1428 99 99 HCFMO54 >sp.vertline.P22033.vertline.MUTA_HUMAN METHYLMALONYL-COA MUTASE
PRECURSOR (EC 5.4.99.2) (MCM). Length = 750 673 841194 (AF039405) arsenite-translocating ATPase [Mus gi.vertline.2745900 182 1138 95 95 HCGAB52 musculus]>sp.vertline.O54984.vertline.O54984 ARSENITE- TRANSLOCATING ATPASE. Length = 350 674 841195 3 623 HCEWM29 675 841198 2 913 HCFBC32 676 841200 (AF015037) **endooligopeptidase** A related gi.vertline.2827886 35 703 75 81 HCEER84 protein; EOPA related protein [Oryctolagus cuniculus]>sp.vertline.O46480.vertline.O46480 **ENDOOLIGOPEPTIDASE** A RELATED PROTEIN (FRAGMENT). Length = 667 677 841201 158 571 HCEBD63 678 841202 rhoB [Homo sapiens]>gi.vertline.206656 rhoB [Rattus gi.vertline.36032 66 1229 100 100 HCHOV21 norvegicus]>gnl.vertline.PID.vertline.e258480 RHOB [Mus musculus]>pir.vertline.A01372.vertline.TVHURH GTP-binding protein rhoB-human >pir.vertline.A39727.vertline.- TVRTRH GTP-binding protein rhoB-rat >pir.vertline.JC5075.vertline.JC5075 GTP-binding protein rhoB-mouse >gi.vertline.3373 679 841209 1 552 HCDMF27 680 841210 PTB-associated splicing factor [Homo sapiens] gi.vertline.38458 2 1405 93 93 HCEMT64 >pir.vertline.A46302.v- ertline.A46302 PTB-associated splicing factor, long form-human >gi.vertline.23712 myoblast antigen 24.1D5 [Homo sapiens] [SUB 312-707] >gi.vertline.4063717 (AF110499) PTB-associated splicing factor [Mus musculus] [SUB 377 681 841213 G9a [Homo sapiens]>pir.vertline.530385.vertline.530385 G9a gi.vertline.287865 3 344 82 84 HCEFE38 protein-human >sp.vertline.Q14349.vertline.Q14349 G9A PROTEIN CONTAINING ANKYRIN-LIKE REPEATS. Length = 1001 682 841217 2 1198 HCE1V79 683 841219 SMOOTH MUSCLE MYOSIN HEAVY CHAIN sp.vertline.D1037960.vertline.D1037960 208 774 95 97 HBZSI02 (FRAGMENT). Length = 1052 684 841222 29 856 HCDCI63 685 841223 2088 2486 HCEBW38 686 841224 RNA polymerase II elongation factor ELL2 gi.vertline.1946347 2 2032 95 95 HCE2D15 [Homo sapiens]>sp.vertline.O00472.vertline.ELL2_HUMAN RNA

POLYMERASE II ELONGATION FACTOR ELL2. Length = 640 687 841226 2 373 HCCMD50
688 841227 1 831 HBZAK55 689 841228 F25H9.7 [Caenorhabditis elegans]
gnl.vertline.PID.vertline.e134600- 3 3 407 46 62 HCDEA07
>gnl.vertline.PID.vertline.e1346003 F25H9.7 [Caenorhabditis
elegans]>sp.vertline.P91989.vertline.- P91989 F25H9.7 PROTEIN. Length =
154 690 841231 279 977 HBXCC66 691 841232 MHC HLA-RD protein [Homo sapiens]
gi.vertline.386949 3 461 94 95 HCE1S91 >pir.vertline.A33640.v-
ertline.A33640 class III histocompatibility antigen RD-human Length = 382
692 841233 (AF069984) nitrilase homolog 1 [Homo sapiens] gi.vertline.3242978 2
673 94 95 HBUAF56 >gi.vertline.3228666 (AF069987) nitrilase 1 [Homo
sapiens]>sp.vertline.O76091.vertline.O76091 NITRILASE HOMOLOG 1. Length =
327 693 841234 (AJ005073) Alix [Mus musculus]
gnl.vertline.PID.vertline.e1318710 561 2564 89 91 HBWCI70
>sp.vertline.O88695.vertline.O88695 ALIX. Length = 869 694 841236 187 483
HBXGB85 695 841238 168 389 HBXFF92 696 841239 405 605 HBMUU08 697 841242 169
360 HBNAT03 698 841243 3 281 HBMTQ45 699 841248 phorbolin 3 [Homo sapiens]
gi.vertline.4097433 3 668 46 62 HBUAC02
>sp.vertline.G4097433.vertline.G4097433 PHORBOLIN 3. Length = 235 700
841250 2 1309 HBJEC31 701 841251 5 247 HBJLL24 702 841254 879 1136 HBZSH07
703 841263 1 354 HBJDS57 704 841266 182 337 HBJFN11 705 841269 (AL021958)
fadE9 [Mycobacterium tuberculosis] gnl.vertline.PID.vertline.e- 1253290 93
1130 51 70 HBDAC79 >sp.vertline.O53815.vertline.O53- 815 ACYL-COA
DEHYDROGENASE. Length = 390 706 841272 p67 myc protein [Homo sapiens]
gnl.vertline.PID.vertline.d1001846 20 622 100 100 HBJFJ36
>sp.vertline.D1001846.vertline.D1001846 P67 MYC PROTEIN (FRAGMENT). Length
= 454 707 841273 697 948 HBFMD57 708 841276 244 423 HBNAE62 709 841277
NADH-UBIQUINONE OXIDOREDUCTASE sp.vertline.Q16795.vertline.NUEM_H 2 1171 94 94
HBICG75 39 KD SUBUNIT PRECURSOR (EC 1.6.5.3) UMAN (EC 1.6.99.3) (COMPLEX
I-39KD) (CI-39KD). >gi.vertline.189049 NADH dehydrogenase (ubiquinone)
[Homo sapiens] [SUB 3-377] Length = 377 710 841278 gag polyprotein-human
endogenous virus S71 pir.vertline.A46312.vertline.A46312 119 415 44 56 HATDB46
Length = 608 711 841279 187 645 HPIAF81 712 841280 (AF061513) candidate
adaptor protein CED-6 gi.vertline.3253308 888 1823 50 69 HBCAS37
[Caenorhabditis elegans]>sp.vertline.O76337.vertline.- O76337 CANDIDATE
ADAPTOR PROTEIN CED-6. Length = 492 713 841282 219 368 HATAM48 714 841283
2530 2880 HBAFS89 715 841286 (AC003096) putative protein phosphatase 2C
gi.vertline.3132471 201 1319 57 80 HAHCP59 [Arabidopsis
thaliana]>sp.vertline.O64583.vertline.O64583 HYPOTHETICAL 26.4 KD PROTEIN.
Length = 239 716 841287 3 248 HARMV18 717 841288 (AL021428) hypothetical
protein Rv0068 gnl.vertline.PID.vertline.e1245998 3 821 HARMM85
[Mycobacterium tuberculosis] >sp.vertline.O53613.vertline.O53- 613
OXIDOREDUCTASE. Length = 303 718 841291 selenoprotein P [Homo sapiens]
Length = 381 gnl.vertline.PID.vertline.e1192260 293 1012 88 89 HBMCL13 719
841292 SSR gamma subunit [Rattus norvegicus] gi.vertline.312702 2 664 98 98
HARAI52 >pir.vertline.533294.v- ertline.533294 translocon-associated
protein gamma chain-rat Length = 185 720 841294 microtubule associated
protein [Homo sapiens] gi.vertline.414115 3 1265 99 99 HAPOR25
>pir.vertline.I37356.vertline.I37356 epithelial microtubule- associated
protein, 115K-human >sp.vertline.Q14244.vertline.Q-

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ABSTRACT:

Compositions and methods for the therapy and diagnosis of cancer, such as ovarian cancer, are disclosed. Compositions may comprise one or more ovarian carcinoma proteins, immunogenic portions thereof, polynucleotides that encode such portions or antibodies or immune system cells specific for such proteins. Such compositions may be used, for example, for the prevention and treatment of diseases such as ovarian cancer. Methods are further provided for identifying tumor antigens that are secreted from ovarian carcinomas and/or other tumors. Polypeptides and polynucleotides as provided herein may further be used for the diagnosis and monitoring of ovarian cancer.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a CIP of U.S. application Ser. No. 09/397,787 filed Sep. 16, 1999 (pend.), which is a CIP of U.S. application Ser. No. 09/246,429 filed Feb. 8, 1999 (ab.), which is a CIP of U.S. application Ser. No. 09/159,320 filed Sep. 23, 1998 (ab.), all incorporated in their entirety herein by reference.

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Detail Description Table CWU - DETL:

3TABLE III Further Ovarian Carcinoma Antigen Partial Sequences SEQ ID Clone No. Sequence NO Homology OVp2-3 15674.2 130 Novel OVp2-8 15679.2 131 A. t BAC F21E10; ESTs OVp2-26 20045.1 132 Human I-mf; ETS OVp2-33 20047.1 133 Novel; ESTs OVp2-34 20056.1 134 BiP, GRP; ESTs OVp2-45 17295.1 135 Human Chrom 16; ESTs OVp2-49 20209.1 136 Human C90RF3 short isoform; ESTs OVp2-53 16111.2 137 Novel; ESTs OVp2-61 22421.1 138 Novel OVp2-62 22422.1 139 TNF-.alpha. stimulated ATP-binding; ESTs OVp2-63 22423.1 140 Human.DNA from phage pTELchrom. 16p13.3; ESTs OVp2-64 22424.1 141 Human mRNA for fibronectin; ESTs OVp2-65 22425.1 142 Novel; ESTs OVp2-74 22428.1 143 Human deoxyhypusine synthase mRNA; ESTs OVp2-75 22430.1 144 Novel OVp2-76 22431.1 145 Novel; ESTs OVp2-77 22432.1 146 Novel; ESTs OVp2-78 22433.1 147 Human.cDNA DKFZp586E0518; ESTs OVp2-79 22434.1 148 Human DNA cosmid U131B10 OVp2-95 20213.1 149 Hu. Protective protein; ESTs OVp2-97 20214.1 150 Plasma protein S; ESTs OVp2-107 20216.1 151 Human epiderm al carcinoma mRNA for E2; ESTs OVp2-113 20496.1 152 Human Histone H1'; ESTs OVp2-114 20497.1 153 Novel OVp2-116 18077.1 154 Human Pyruvate dehydrogenase kinase; EST OVp2-119 18078.1 155 Human KIAA0803, BAC clone; ESTs OVp2-121 20498.1 156 Murine DNA-binding, Zn Finger; ESTs OVp2-122 18085.1 157 Rat trg OVp2-124 20500.1 158 Novel; ESTs OVp2-127 18084.1 159 Human Cosmid F23149 OVp2-128 20501.1 160 Human GlcNac 1-P transferase; ESTs OVp2-129 20502.1 161 Novel; EST OVp2-131 18573.2 162 Human laminin alpha 5 chain; ESTs OVp2-133 18574.1 163 Novel OVp2-134 18345.1 164 Human tazarotene-induced gene 2; ESTs OVp2-135 18575.1 165 Actin-binding P57, coronin-like; ESTs OVp2-139 18728.1 166 Human clone 1033D10; includes BING5; ESTs OVp2-141 18577.1 167 Human cosmid F23149; EST OVp2-143 18881.1 168 c-myc proto-oncogene; ESTs OVp2-144 18882.1 169 Murine, Human nucleic acid-binding protein; ESTs OVp2-146 18884.1 170 Novel; ESTs OVp2-147 18885.1 171 Human B23 nucleophosmin; ESTs OVp2-148 18886.1 172 cation-dependent Human,Murine MP-6R; ESTs OVp2-150 18889.1 173 Human FXR1; ESTs OVp2-152 18891.1 174 Human KIAA0465; ESTs OVp2-153 18892.1 175 Human .alpha.-2macroglobin receptor assoc; ESTs OVp2-158 20027.1 176 Topoisomerase II; ESTs OVp2-160 20028.1 177 Novel OVp2-162 20029.1 178 Novel OVp2-167 20035.1 179 KIAA0630; ESTs OVp2-169 20037.1 180 Novel OVp2-171 20039.1 181 Novel; ESTs OVp2-172 20072.1 182 Novel OVp2-174 20031.1 183 mig-2; ESTs OVp2-179 20040.1 184 Novel; ESTs OVp2-180 20041.1 185 Antiquin; turgor protein; ESTs OVp2-184 20044.1 186 Human ribosomal P1; ESTs OVp2-185 20057.1 187 Novel; ESTs OVp2-187 20074.1 188 MuLV env OVp2-188 20075.1 189 Novel; EST OVp2-189 20058.1 190 Novel; EST OVp2-190 20059.1 191 Gonadotropin-Reg Hormone Producing; ESTs OVp2-191 21502.1 192 Novel; ESTs OVp2-192 21503.1 193 18S rRNA, DNA; ESTs OVp2-193 21504.1 194 Arg-rich Nuclear Protein; ESTs OVp2-194 21505.1 195 Novel; ESTs OVp2-195 21506.1 196 Novel; ESTs OVp2-196 21507.1 197 Human Clone 406A7; ESTs OVp2-197 21508.1 198 Novel; ESTs OVp2-204 22128.1 199 Human Mitochondrial DNA; ESTs OVp2-206 22129.1 200 Human chrom. DNA for RAD23A; ESTs OVp2-207 22130.1 201 Human clone 24921 mRNA; ESTs OVp2-208 22131.1 202 Human 4F5rel mRNA; ESTs OVp2-209 22133.1 203 Human ribosomal pro. S6 kinase.SW1/SNF related; ESTs OVp2-211 22134.1 204 Human beta-glucuronidase (BG) mRNA; ESTs OVp2-212 22135.1 205 Human DNA for hnRNP protein A2/B1; ESTs OVp2-215 22137.1 206 Human translocation protein 1; ESTs

OVp2-216 22138.1 207 Human chromosone X orf5; ESTs OVp2-217 22139.1 208 Human ribosomal protein S19; ESTs OVp2-218 22140.1 209 Murine mRNA for histone H3.3A; ESTs OVp2-220 22141.1 210 Human PAC 434P1; ESTs OVp2-221 22142.1 211 Human AKAP450.KIAA0803.Hyper- ion; ESTs OVp2-222 22144.1 212 Human HRFX2 mRNA, DNA binding OVp2-223 22145.1 213 Human NF-kappa-B transcrip'n factor p65; ESTs OVp2-225 22146.1 214 Novel OVp2-226 22147.1 215 Novel OVp2-228 22148.1 216 Novel; ESTs OVp2-229 22149.1 217 Human mitochondrial genes; ESTs OVp2-230 22150.1 218 O. cuniculus **endooligopeptidase** A related protein; ESTs OVp2-232 22152.1 219 Human clone A9A2BR11; Mu Zfr OVp2-233 22153.1 220 Human KIAA0098; Murine chaperonin containing TCP-1; ESTs OVp2-238 22154.1 221 human DNA seq. from PAC 93H18; ESTs OVp2-239 22155.1 222 Novel OVp2-241 22156.1 223 Human glutathione S-transferase theta 1; ESTs OVp2-243 22157.1 224 Human TCB.OIP3, pyruvate kinase; ESTs OVp2-244 22158.1 225 Human mRNA for KIAA0250 gene; EST OVp2-250 22160.1 226 Human complement component C4A mRNA; EST OVp2-251 22161.1 227 Novel; EST OVp2-252 22162.1 228 Novel; EST OVp2-253 22163.1 229 Human. G protein Golf alpha gene; ESTs OVp2-254 22164.1 230 Novel; ESTs OVp2-257 22897.1 231 Novel; ESTs OVp2-258 22440.1 232 Human chrom 16. cosmid clone 399H11; ESTs OVp2-259 22441.1 233 human cDNA DKFZp564B112; ESTs OVp2-260 22898.1 234 Novel; ESTs OVp2-262 22442.1 235 Human mRNA for ribosomal protein L31; ESTs OVp2-265 22899.1 236 Human TNF receptor mRNA; ESTs OVp2-266 22445.1 237 Human 12q13.1 PAC RPCI1-228P16 OVp2-270 22447.1 238 Hu. cDNA DKFZp586F1523; ESTs OVp2-273 22450.1 239 Homo sapiens cytochrome b-245; ESTs OVp2-276 22451.1 240 Novel; ESTs OVp2-279 22454.1 241 Novel; ESTs OVp2-282 22903.1 242 Novel; ESTs OVp2-283 22904.1 243 Human KIAA9001 mRNA,RING3; ESTs OVp2-284 22905.1 244 Novel; ESTs OVp2-285 22906.1 245 Novel; ESTs OVp2-287 22907.1 246 Novel OVp3-15 20048.1 247 JM26; ESTs OVp3-27 20049.1 248 mult. Human BAC; Line1; ESTs OVp3-42 20050.1 249 Tyrosine phosphatase; ESTs OVp3-58 20052.1 250 Novel; ESTs OVp3-61 20060.1 251 Novel; ESTs OVp3-73 20064.1 252 glypican-4 OVp3-74 20065.1 253 Novel; ESTs OVp3-78 20069.1 254 Novel OVp3-80 20053.1 255 MLN 50 RNA; EST OVp3-89 20217.1 256 Novel OVp3-108 20222.1 257 Human parathymosin; ESTs OVp3-109 20223.1 258 Human eryth/.alpha.-adductin; ESTs OVp3-114 18080.1 259 Novel OVp3-115 20225.1 260 Human JM26; ESTs OVp3-116 20226.1 261 Novel; ESTs OVp3-120 20503.1 262 Human KIAA0875; ESTs OVp3-121 20227.1 263 Human Guanine-binding; ESTs OVp3-122 20228.1 264 Novel; ESTs OVp3-123 18086.1 265 Novel OVp3-124 18087.1 266 Human transposon L1.2; ESTs OVp3-127 18089.1 267 low sim. to Mu.Hepatoma GF; ESTs OVp3-129 20504.1 268 Human .beta. spectrin (actin-binding); ESTs OVp3-130 18347.1 269 BAC GS083B20; Line1, p150; ESTs OVp3-131 18348.1 270 glutathione S-transferase; ESTs OVp3-132 18349.1 271 Human mRNA KIAA0710; EST OVp3-136 20506.1 272 Novel; ESTs OVp3-137 18731.1 273 Novel; ESTs OVp3-142 20508.1 274 Novel OVp3-144 18735.1 275 Novel; EST OVp3-147 18738.1 276 KIAA0941,PGEMEX; ESTs OVp3-148 20510.1 277 Polyubiquitin; ESTs OVp3-149 18894.1 278 Novel; ESTs OVp3-150 18895.1 279 Human SWI/SNF; ESTs OVp4-1 20017.1 280 Novel; EST OVp4-2 20018.1 281 Human KIAA0241; ESTs

US-PAT-NO: 6468758

DOCUMENT-IDENTIFIER: US 6468758 B1

TITLE: Compositions and methods for ovarian cancer therapy and diagnosis

DATE-ISSUED: October 22, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Benson; Darin R.	Seattle	WA	N/A	N/A
Lodes; Michael J.	Seattle	WA	N/A	N/A
Mitcham; Jennifer L.	Redmond	WA	N/A	N/A
King; Gordon E.	Seattle	WA	N/A	N/A

APPL-NO: 09/ 397787

DATE FILED: September 16, 1999

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of U.S. application Ser. No. 09/246,429, filed Feb. 8, 1999, which is a continuation-in-part of U.S. application Ser. No. 09/159,320 filed Sep. 23, 1998, now abandoned.

US-CL-CURRENT: 435/7.23; 435/6 ; 536/24.31

ABSTRACT:

Compositions and methods for the therapy and diagnosis of cancer, such as ovarian cancer, are disclosed. Compositions may comprise one or more ovarian carcinoma proteins, immunogenic portions thereof, polynucleotides that encode such portions or antibodies or immune system cells specific for such proteins. Such compositions may be used, for example, for the prevention and treatment of diseases such as ovarian cancer. Methods are further provided for identifying tumor antigens that are secreted from ovarian carcinomas and/or other tumors. Polypeptides and polynucleotides as provided herein may further be used for the diagnosis and monitoring of ovarian cancer.

3 Claims, 32 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 32

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Detailed Description Paragraph Table - DETL:

TABLE III Further Ovarian Carcinoma Antigen Partial Sequences Clone No. Sequence SEQ ID NO Homology OVp2-3 15674.2 130 Novel OVp2-8 15679.2 131 A.t BAC F21E10; ESTs OVp2-26 20045.1 132 Human 1-mf; ETS OVp2-33 20047.1 133 Novel; ESTs OVp2-34 20056.1 134 BiP, GRP; ESTs OVp2-45 17295.1 135 Human Chrom 16; ESTs OVp2-49 20209.1 136 Human C90RF3 short isoform; ESTs OVp2-53 16111.2 137 Novel; ESTs OVp2-61 22421.1 138 Novel OVp2-62 22422.1 139 TNF-.alpha. stimulated ATP-binding; ESTs OVp2-63 22423.1 140 Human.DNA from phage pTELchrom. 16p13.3; ESTs OVp2-64 22424.1 141 Human mRNA for fibronectin; ESTs OVp2-65 22425.1 142 Novel; ESTs OVp2-74 22428.1 143 Human deoxyhypusine synthase mRNA; ESTs OVp2-75 22430.1 144 Novel OVp2-76 22431.1 145 Novel; ESTs OVp2-77 22432.1 146 Novel; ESTs OVp2-78 22433.1 147 Human.cDNA DKFZp586E0518; ESTs OVp2-79 22434.1 148 Human DNA cosmid U131B10 OVp2-95 20213.1 149 Hu. Protective protein; ESTs OVp2-97 20214.1 150 Plasma protein S; ESTs OVp2-107 20216.1 151 Human epiderm al carcinoma mRNA for E2; ESTs OVp2-113 20496.1 152 Human Histone H1'; ESTs OVp2-114 20497.1 153 Novel OVp2-116 18077.1 154 Human Pyruvate dehydrogenase kinase; EST OVp2-119 18078.1 155 Human K1AA0803, BAC clone; ESTs OVp2-121 20498.1 156 Murine DNA-binding, Zn Finger; ESTs OVp2-122 18085.1 157 Rat trg OVp2-124 20500.1 158 Novel; ESTs OVp2-127 18084.1 159 Human Cosmid F23149 OVp2-128 20501.1 160 Human GlcNac 1-P transferase; ESTs OVp2-129 20502.1 161 Novel; EST OVp2-131 18573.2 162 Human laminin alpha 5 chain; ESTs OVp2-133 18574.1 163 Novel OVp2-134 18345.1 164 Human tazarotene-induced gene 2; ESTs OVp2-135 18575.1 165 Actin-binding P57, coronin-like; ESTs OVp2-139 18728.1 166 Human clone 1033D10; includes BING5; ESTs OVp2-141 18577.1 167 Human cosmid F23149; EST OVp2-143 18881.1 168 c-myc proto-oncogene; ESTs OVp2-144 18882.1 169 Murine, Human nucleic acid-binding protein; ESTs OVp2-146 18884.1 170 Novel; ESTs OVp2-147 18885.1 171 Human B23 nucleophosmin; ESTs OVp2-148 18886.1 172 cation-dependent Human, Murine MP-6R; ESTs OVp2-150 18889.1 173 Human FXR1; ESTs OVp2-152 18891.1 174 Human KIAA0465; ESTs OVp2-153 18892.1 175 Human .alpha.-2macroglobin receptor assoc; ESTs OVp2-158 20027.1 176 Topoisomerase II; ESTs OVp2-160 20028.1 177 Novel OVp2-162 20029.1 178 Novel OVp2-167 20035.1 179 K1AA0630; ESTs OVp2-169 20037.1 180 Novel OVp2-171 20039.1 181 Novel; ESTs OVp2-172 20072.1 182 Novel OVp2-174 20031.1 183 mig-2; ESTs OVp2-179 20040.1 184 Novel; ESTs OVp2-180 20041.1 185 Antiquin; turgor protein; ESTs OVp2-184 20044.1 186 Human ribosomal P1; ESTs OVp2-185 20057.1 187 Novel; ESTs OVp2-187 20074.1 188 MuLV env OVp2-188 20075.1 189 Novel; EST OVp2-189 20058.1 190 Novel; EST OVp2-190 20059.1 191 Gonadotropin-Reg Hormone Producing; ESTs OVp2-191 21502.1 192 Novel; ESTs OVp2-192 21503.1 193 18S rRNA, DNA; ESTs OVp2-193 21504.1 194 Arg-rich Nuclear Protein; ESTs OVp2-194 21505.1 195 Novel; ESTs OVp2-195 21506.1 196 Novel; ESTs OVp2-196 21507.1 197 Human Clone 406A7; ESTs OVp2-197 21508.1 198 Novel; ESTs OVp2-204 22128.1 199 Human Mitochondrial DNA; ESTs OVp2-206 22129.1 200 Human chrom. DNA for RAD23A; ESTs OVp2-207 22130.1 201 Human clone 24921 mRNA; ESTs OVp2-208 22131.1 202 Human 4F5rel mRNA; ESTs OVp2-209 22133.1 203 Human ribosomal pro. S6 kinase.SW1/SNF related; ESTs OVp2-211 22134.1 204 Human beta-glucuronidase (BG) mRNA; ESTs OVp2-212 22135.1 205 Human DNA for hnRNP protein A2/B1; ESTs OVp2-215 22137.1 206 Human translocation protein 1; ESTs OVp2-216 22138.1 207 Human chromosone X orf5; ESTs OVp2-217 22139.1 208 Human ribosomal protein S19; ESTs OVp2-218 22140.1 209 Murine mRNA for histone H3.3A; ESTs OVp2-220 22141.1 210 Human PAC 434P1; ESTs OVp2-221 22142.1 211 Human AKAP450.K1AA0803.Hyperion; ESTs OVp2-222 22144.1 212 Human HRFX2 mRNA, DNA

binding OVp2-223 22145.1 213 Human NF-kappa-B transcrip'n factor p65; ESTs OVp2-225 22146.1 214 Novel OVp2-226 22147.1 215 Novel OVp2-228 22148.1 216 Novel; ESTs OVp2-229 22149.1 217 Human mitochondrial genes; ESTs OVp2-230 22150.1 218 O. cuniculus **endoolig peptidase** A related protein; ESTs OVp2-232 22152.1 219 Human clone A9A2BR11; Mu Zfr OVp2-233 22153.1 220 Human KIAA0098; Murine chaperonin containg TCP-1; ESTs OVp2-238 22154.1 221 human DNA seq. from PAC 93H18; ESTs OVp2-239 22155.1 222 Novel OVp2-241 22156.1 223 Human glutathione S-transferase theta 1; ESTs OVp2-243 22157.1 224 Human TCB.OIP3, pyruvate kinase; ESTs OVp2-244 22158.1 225 Human mRNA for KIAA0250 gene; EST OVp2-250 22160.1 226 Human complement component C4A mRNA; EST OVp2-251 22161.1 227 Novel; EST OVp2-252 22162.1 228 Novel; EST OVp2-253 22163.1 229 Human. G protein Golf alpha gene; ESTs OVp2-254 22164.1 230 Novel; ESTs OVp2-257 22897.1 231 Novel; ESTs OVp2-258 22440.1 232 Human chrom 16. cosmid clone 399H11; ESTs OVp2-259 22441.1 233 human cDNA DKFZp564B112; ESTs OVp2-260 22898.1 234 Novel; ESTs OVp2-262 22442.1 235 Human mRNA for ribosomal protein L31; ESTs OVp2-265 22899.1 236 Human TNF receptor mRNA; ESTs OVp2-266 22445.1 237 Human 12q13.1 PAC RPC11-228P16 OVp2-270 22447.1 238 Hu. cDNA DKFZp586F1523; ESTs OVp2-273 22450.1 239 Homo sapiens cytochrome b-245; ESTs OVp2-276 22451.1 240 Novel; ESTs OVp2-279 22454.1 241 Novel; ESTs OVp2-282 22903.1 242 Novel; ESTs OVp2-283 22904.1 243 Human K1AA9001 mRNA,R1N63; ESTs OVp2-284 22905.1 244 Novel; ESTs OVp2-285 22906.1 245 Novel; ESTs OVp2-287 22907.1 246 Novel OVp3-15 20048.1 247 JM26; ESTs OVp3-27 20049.1 248 mult. Human BAC; Linel; ESTs OVp3-42 20050.1 249 Tyrosine phosphatase; ESTs OVp3-58 20052.1 250 Novel; ESTs OVp3-61 20060.1 251 Novel; ESTs OVp3-73 20064.1 252 glypican-4 OVp3-74 20065.1 253 Novel; ESTs OVp3-78 20069.1 254 Novel OVp3-80 20053.1 255 MLN 50 RNA; EST OVp3-89 20217.1 256 Novel OVp3-108 20222.1 257 Human parathymosin; ESTs OVp3-109 20223.1 258 Human eryth/.alpha.-adductin; ESTs OVp3-114 18080.1 259 Novel OVp3-115 20225.1 260 Human JM26; ESTs OVp3-116 20226.1 261 Novel; ESTs OVp3-120 20503.1 262 Human K1AA0875; ESTs OVp3-121 20227.1 263 Human Guanine-binding; ESTs OVp3-122 20228.1 264 Novel; ESTs OVp3-123 18086.1 265 Novel OVp3-124 18087.1 266 Human transposon L1.2; ESTs OVp3-127 18089.1 267 low sim. to Mu. Hepatoma GF; ESTs OVp3-129 20504.1 268 Human .beta. spectrin (actin-binding); ESTs OVp3-130 18347.1 269 BAC GS083B20; Linel, p150; ESTs OVp3-131 18348.1 270 glutathione S-transferase; ESTs OVp3-132 18349.1 271 Human mRNA KIAA0710; EST OVp3-136 20506.1 272 Novel; ESTs OVp3-137 18731.1 273 Novel; ESTs OVp3-142 20508.1 274 Novel OVp3-144 18735.1 275 Novel; EST OVp3-147 18738.1 276 K1AA0941, PGEMEX; ESTs OVp3-148 20510.1 277 Polyubiquitin; ESTs OVp3-149 18894.1 278 Novel; ESTs OVp3-150 18895.1 279 Human SWI/SNF; ESTs OVp4-1 20017.1 280 Novel; EST OVp4-2 20018.1 281 Human KIAA0241; ESTs OVp4-4 20019.1 282 Novel; ESTs OVp4-6 20020.1 283 Novel; ESTs OVp4-7 20021.1 284 laminin-binding; ESTs OVp4-8 20022.1 285 okadaic-acid-inducible; ESTs OVp4-10 20023.1 286 MAC25; ESTs OVp4-13 20054.1 287 Novel; ESTs OVp4-14 20055.1 288 Novel OVp4-15 20076.1 289 Human HSP; ESTs OVp4-16 20077.1 290 Clathrin; .delta.3A (AP-3 complex); ESTs OVp4-18 20078.1 291 Novel; ESTs OVp4-20 20070.1 292 Novel OVp4-22 20229.1 293 Human .beta.-Catenin; ESTs OVp4-22A 20511.1 294 IIPPL1 (51C); DNA repair; ESTs OVp4-23 20230.1 295 Transcrp'n Fact. AP-1, JUN A, C-JUN; ESTs OVp4-24 20231.1 296 Novel; ESTs OVp4-25 20512.1 297 Novel; ESTs OVp4-26 20232.1 298 ribosomal P0; ESTs OVp4-26A 20538.1 299 Novel; ESTs OVp4-28 20234.1 300 Transcrp'n Factor S-II; ESTs OVp4-29 20235.1 301 Novel; ESTs OVp4-30 20236.1 302 Human AHNAK; neuroblast diff'n.; ESTs OVp4-31 20237.1 303 CD81(TAPA-1) cell surface; ESTs OVp4-33 20545.1 304 Novel; ESTs OVp4-34 20546.1 305 Novel OVp4-35 20547.1 306 Novel;

ESTs OVp4-36 21510.1 307 Novel OVp4-37 20548.1 308 Novel; ESTs OVp4-38 22166.1 309 Novel; ESTs OVp4-40 20549.1 310 Human Profilin; EST OVp4-43 20551.1 311 Novel OVp4-44 20552.1 312 Human 30M3; ESTs OVp4-45 20553.1 313 Chrom. 14 specific cosmid OVp4-46 20554.1 314 Novel; ESTs OVp4-47 20555.1 315 EF-1 .alpha.; ESTs OVp4-48 20556.1 316 B-CAM mRNA; EST OVp4-49 20557.1 317 Novel OVp4-51 20559.1 318 Human N-cadherin; ESTs OVp4-52 20560.1 319 Human p16INK4/MTS1; ESTs OVp4-53 20561.1 320 Human RNA helicase OVp4-54 20562.1 321 Murine Fibronectin; ESTs OVp4-55 20778.1 322 RibosomalS6(kinase substrate); ESTs OVp4-56 20779.1 323 Novel; ESTs OVp4-58 20781.1 324 CPG island DNA; EST OVp4-59 20782.1 325 Human KIAA 0241; ESTs OVp4-61 20784.1 326 Human PAC; EST OVp4-62 20785.1 327 Na/H reg. factor; ESTs OVp4-63 20786.1 328 Ferritin Heavy Chain; ESTs OVp4-64 20787.1 329 MHC -1 H2; ESTs OVp4-66 20789.1 330 RNA Helicase-related; ESTs OVp4-70 20793.1 331 BC-2protein RNA; ESTs OVp4-72 20795.1 332 Phosphorylase Kinase; ESTs OVp4-73 20796.1 333 Novel OVp4-74 20797.1 334 Human clone 327J16; ESTs

US-PAT-NO: 6291201

DOCUMENT-IDENTIFIER: US 6291201 B1

TITLE: Fluorescence energy transfer substrates

DATE-ISSUED: September 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Garman; Andrew John	Chester	N/A	N/A	GB

APPL-NO: 08/ 557005

DATE FILED: November 17, 1995

PARENT-CASE:

This application claims benefit of international application PCT/GB94/01153, filed May 27, 1994.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
GB	9310978	May 27, 1993

PCT-DATA:
APPL-NO: PCT/GB94/01153
DATE-FILED: May 27, 1994
PUB-NO: WO94/28166
PUB-DATE: Dec 8, 1994
371-DATE: Nov 17, 1995
102(E)-DATE: Nov 17, 1995

US-CL-CURRENT: 435/23; 435/212 ; 435/219 ; 435/24 ; 435/968 ; 530/300 ; 530/333 ; 530/334 ; 530/402

ABSTRACT:

A method for the preparation of a fluorescence resonance energy transfer (FRET) substrate having donor and acceptor species on opposite sides of a proteolytic cleavage site and wherein the donor and/or acceptor species are attached via the side chain(s) of amino acid(s) therein. The method comprises contacting a reactive donor or acceptor species with a polypeptide substrate having the side chain(s) of amino acid(s) therein adapted for reaction with the reactive species and then contacting the substrate so obtained with a corresponding reactive donor or acceptor species. Novel FRET substrates so prepared and their use in assays to identify modulators of protease activity.

18 Claims, 2 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 2

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Other Reference Publication - OREF:

Juliano et al., "A Selective Assay for **Endooligopeptidase** A Based on the Cleavage of Fluorogenic Substrate Structurally Related to Enkephlin", Biochem. Biophys. Res. Comm., 173(2), pp. 647-652, Dec. 1990.*

US-PAT-NO: 6171790

DOCUMENT-IDENTIFIER: US 6171790 B1

TITLE: Human protease associated proteins

DATE-ISSUED: January 9, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hillman; Jennifer L.	Mountain View	CA	N/A	N/A
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Lal; Preeti	Sunnyvale	CA	N/A	N/A
Corley; Neil C.	Mountain View	CA	N/A	N/A
Guegler; Karl J.	Menlo Park	CA	N/A	N/A
Patterson; Chandra	Mountain View	CA	N/A	N/A

APPL-NO: 09/ 071709

DATE FILED: May 1, 1998

US-CL-CURRENT: 435/6; 435/226 ; 435/252.3 ; 435/320.1 ; 435/325 ; 435/69.1 ; 536/23.1 ; 536/23.2 ; 536/23.5

ABSTRACT:

The invention provides human protease associated proteins (HPRAP) and polynucleotides which identify and encode HPRAP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders associated with expression of HPRAP.

15 Claims, 30 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 30

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Drawing Description Text - DRTX:

FIGS. 5A, 5B, 5C, and 5D show the amino acid sequence alignments between HPRAP-1 (031381; SEQ ID NO:1) and an **endooligopeptidase** A related protein from Oryctolagus cuniculus (GI 2827886; SEQ ID NO:9), produced using the multisequence alignment program of LASERGENE software (DNASTAR Inc, Madison Wis.).

Detailed Description Text - DETX:

In one embodiment, the invention encompasses a polypeptide comprising the amino acid sequence of SEQ ID NO:1, as shown in FIGS. 1A, 1B, 1C, 1D, 1E, and 1F. HPRAP-1 is 460 amino acids in length and has a potential N-glycosylation site at residue N299, and potential phosphorylation sites for cAMP- and cGMP-dependent protein kinase at T132, for casein kinase II at S11, S29, S95, S135, S155, and S310, for protein kinase C at S11, S23, S90, T191, S231, S247, S282, S331, S344, and S404, and for tyrosine kinase at Y87. As shown in FIGS. 5A, 5B, 5C, and 5D, HPRAP-1 has chemical and structural similarity with an **endooligopeptidase** A related protein from O. cuniculus (GI 2827886; SEQ ID NO:9). In particular, HPRAP-1 and the **endooligopeptidase** A related protein share 89% identity, including the potential N-glycosylation site and most of the potential phosphorylation sites found in HPRAP-1. The fragment of SEQ ID NO:5 from about nucleotide 1152 to about nucleotide 1205 is useful, for example, as a hybridization probe. Northern analysis shows the expression of this sequence in various libraries, at least 48% of which are immortalized or cancerous and at least 36% of which involve immune response. Of particular note is the expression of HPRAP-1 in cardiovascular and gastrointestinal tissues.

Detailed Description Text - DETX:

Chemical and structural similarity exists between HPRAP-1 and an **endooligopeptidase** A related protein from O. cuniculus (GI 2827886). In addition, HPRAP-1 is expressed in cancer and immortalized cell lines and tissues associated with inflammation and the immune response. Therefore, HPRAP-1 appears to play a role in cell proliferative and immune disorders.

Other Reference Publication - OREF:

Hayashi et al., "**Endooligopeptidase** A related protein", EMBL Sequence Database, Jun. 1, 1998, XP002114379, Heidelberg, DE (Accession 046480).